<u>APPROACH TO</u> McGill Journal of Medicine

Hemoptysis

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ABSTRACT

Hemoptysis is the expectoration of blood from the lower airway. A study in the United Kingdom showed that the annual incidence of hemoptysis in primary care is 0.1%. Between 5 and 15% of patients presenting with hemoptysis have a life-threatening hemoptysis.

Approach to hemoptysis can be particularly perplexing for medical students considering the extensive list of differential diagnosis. It is important for physicians to be able to recognize and manage lifethreatening hemoptysis as it is associated with high morbidity and mortality if untreated. Understanding when to further investigate patients at risk of lung cancer can help detect the disease at an earlier stage.

This article begins with a brief introduction to life-threatening and nonlife-threatening hemoptysis and provides a detailed discussion of its management including diagnostic approaches followed by appropriate imaging modalities, laboratory findings, and clinical management. The target audience of this article are medical students at their preclinical or clinical phase.

KEYWORDS Hemoptysis, Diagnosis of hemoptysis, Life-threatening hemoptysis

1 | QUESTION

A 55-year-old woman presents to the clinic with a cough that has produced blood-streaked sputum for the past four days. Associated symptoms include chest pain and subjective fever. She estimated the amount of blood loss to be less than one tablespoon per day. She reports having a previous episode of hemoptysis two months ago, which was diagnosed as bronchitis that resolved after a few days.

She has a previous medical history of hypertension and was recently diagnosed with type 2 diabetes mellitus. She has no known history of rheumatic disease, heart disease, or lung disease. She has a 30 pack-year smoking history and quit smoking 3 years ago. She does not drink alcohol.

Vital signs at the time of presentation were: temperature of 36.7 °C, blood pressure of 132/68mm Hg, heart rate of 74 beats per minute, and oxygen saturation of 98% on room air. Physical examination revealed normal oropharyngeal mucosa with no signs of bleeding or ulceration.

What is the next best next step in the management of this patient?

- (A) Chest radiograph
- (B) Chest CT scan
- (C) Flexible bronchoscopy
- (D) Prescribe an antibiotic and send the patient home
- (E) Order urinalysis and renal function tests

2 | ANSWER

A) The patient is presenting with less than one tablespoon of blood loss per day, indicating non-lifethreatening hemoptysis. Chest-X-ray (CXR) is suggested as a first-line investigation for all patients with hemoptysis. (1) Even if the patient's CXR is normal and the associated symptoms suggest an infectious etiology, the patient should be further evaluated with a computed tomography (CT) scan +/- flexible bronchoscopy. The patient presents with recurrent hemoptysis and lung cancer risk factors (age > 40 and 30 pack-year history of smoking). A study has shown that up to 10% of patients, with risk factors for lung cancer, have normal CXR despite having lung cancer. (2) If the CXR shows an infiltrate, the patient should be treated with antibiotics for pneumonia.

3 | INITIAL APPROACH

The goal of the initial evaluation of hemoptysis includes confirmation of hemoptysis, evaluation of the severity of the bleeding, localization of the origin, and identification of the etiology. (3) The causes of hemoptysis can be divided into five categories: airway diseases, pulmonary parenchymal diseases, pulmonary vascular diseases, bleeding disorders and trauma, and miscellaneous (table 1). (2)

The first step in the initial evaluation of patients with hemoptysis involves **ruling out pseudohemoptysis**. The term hemoptysis refers to expectorated blood originating from the tracheobronchial tree or pulmonary parenchyma. Blood coming from the upper gastrointestinal tract and the upper respiratory tract is called pseudohemoptysis, and can be identified through history and physical examination (Table 2). (4, 5) The second step in the initial evaluation is to **determine** whether the hemoptysis is life-threatening or non-lifethreatening.

4 | APPROACH TO LIFE-THREATENING HEMOPTYSIS

4.1 | Definition of Life-Threatening Hemoptysis

Life-threatening hemoptysis (LTH), also referred to as massive hemoptysis, is defined as hemoptysis that causes airway obstruction, abnormal gas exchange, or hemodynamic instability. Hemoptysis is also considered LTH if there is a loss of volume of at least 150 mL over 24 hours or a bleeding rate of \geq 100 mL/hour. (6) Although any etiology causing non-LTH hemoptysis can lead to LTH, the most common causes are bronchiectasis, bronchogenic cancer, tuberculosis, and fungal infections. (6)

The lung is supplied by the pulmonary (carries blood from the right ventricle to the pulmonary capillaries for oxygenation and carbon dioxide excretion) and the bronchial systems (provides arterial blood to the tracheobronchial tree). (7) In 90% of the cases, LTH arises from the high-pressure bronchial circulation. (7, 8)

4.2 | Supportive Care

Patients with true LTH should be admitted to the intensive care unit. The initial management focuses on airway protection, volume resuscitation, and correcting any bleeding disorders. (9) The main risk to consider is asphyxiation. To protect the airway, the patients must be placed into a lateral decubitus position with the affected lung down in order to isolate the non-bleeding lung and protect it from pooling of blood. To further protect the airway, most patients are intubated with a largebore endotracheal tube, size 8 or above, that can allow the passage of a therapeutic flexible bronchoscope. (6, 8)

Although hemodynamic instability is a rare phenomenon when managing LTH, patients can become

Cause	Etiol	ogies		
Airway disease	 Bronchitis*: Acute or chronic Bronchiectasis* Neoplasm*: Bronchogenic carcinoma*, Bronchial carcinoid tumor, Metastatic cancer to bronchus or trachea Bronchovascular fistula Dieulafoy disease Foreign body in airway Broncholith 			
Pulmonary parenchymal disease	 Infection Pneumonia* Tuberculosis* Lung abscess Mycetoma* (aspergillosis) and other fungal infections Parasitic disease 	 Rheumatic disease Anti-glomerular basement membrane disease (Goodpasture disease) Granulomatosis with polyangiitis and other vasculitides Behçet disease Primary antiphospholipid antibody Systemic lupus erythematosus Other Genetic defect of collagen Thoracic endometriosis 		
Vascular disease	 Pulmonary embolism* Heart failure* (acquired or congenital), Mitral stenosis Pulmonary arteriovenous malformation Pulmonary artery pseudoaneurysm (due to infection, neoplasm, or trauma) Tracheal-arterial fistulae 	 Pulmonary veno-occlusive disease Pulmonary and bronchial artery aneurysms Endometriosis 		
Bleeding disorders trauma	 Bleeding disorders Anticoagulant and antiplatelet medications Disseminated intravascular coagulation (DIC) Platelet dysfunction (e.g. renal failure) Thrombocytopenia (ITP, TTP, HUS) von Willebrand disease 	 Trauma External blunt or penetrating trauma Airway stent Balloon dilation of airway lesion Biopsy Bronchoscopy Endotracheal tube erosion Transthoracic needle aspiration or biopsy Pulmonary artery catheter 		
Miscellaneous	Drugs and toxins • Cocaine use, Argemone alkaloid- contaminated cooking oil, Bevacizumab treatment, Nitrogen dioxide toxicity, Hy- dralazine (hydralazine-induced vasculitis), Riociguat	 E-cigarette or vaping product use associated lung injury (EVALI) Idiopathic/miscellaneous Idiopathic pulmonary hemosiderosis Amyloid Fibrosing mediastinitis 		

Etiology	History findings	Physical examination	Confirmatory test /
		finding	Procedure
Upper gastrointesti-	Coffee ground appearance,	Epigastric tenderness,	Acidic blood, blood
nal tract	darker blood, black tarry	signs of chronic liver	mixed with food parti-
	stools, nausea & vomiting,	disease	cles, blood in nasogastric
	gastrointestinal disease		aspiration, esophago-
			gastro-duedonoscopy
Upper respiratory	Bleeding gums, epistaxis,	Gingivitis, telangiecta-	Nasopharyngoscopy
tract	little or no cough or spu-	sis, ulceration, varices	
	tum, sore throat	of the tongue, nose, na-	
		sopharynx, oropharynx or	
		hypopharynx	
True Hemoptysis	History suggestive of	Bleeding not coming from	CXR; CT scan; Flexible
	bleeding from the lower	the upper gastrointestinal	bronchoscopy
	respiratory tract including	tract of the upper respira-	
	cough and sputum secre-	tory tract	
	tions; blood may be mixed		
	with sputum		

Information from references 3 and 4

TABLE 2	Differentiating	Features of	Pseudohemoptysis
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tachycardic and hypotensive, requiring hemodynamic resuscitation (7). In addition, bleeding diathesis in patients with suspected bleeding disorders must be managed.

4.3 | Diagnostic Approach

The optimal diagnostic approach to LTH has not been established. (9) In addition, the sequence of the investigations depends upon the stability of the patient. (9) History, physical examination, and CXR, should be done when possible. (6)

Multiple studies suggest that in the setting of LTH, flexible bronchoscopy is the procedure of choice. (6, 7, 9) It can be utilised to remove blood and thrombus, to localize and identify the source of the active bleeding, and to treat the bleeding through a variety of bronchoscopic techniques. (6) In addition to flexible bronchoscopy, a CT of the chest (with and without contrast) is performed to help localize the bleed and identify the etiology. (6, 8)

4.4 | Management of LTH

- Bronchoscopic Interventions Multiple bronchoscopic techniques can be used to control the pulmonary hemorrhage such as iced saline lavage or tranexamic acid, topical medications (vasoconstrictive agents), balloon tamponade or bronchial blockade, and local thermal ablative therapies. (6, 8)
- 2. Bronchial Artery Embolization (BAE) In up to 90% of hemoptysis cases, the bronchial arteries are the source of the bleed. First, arteriography is performed in order to search for abnormal vascular structure or a hypervascularized site with tortuous vessels. Embolization is achieved by inserting occlusive material into the pathological vessel or the one supplying it, in order to stop the bleeding. (6, 8)
- **3. Surgical Treatment** Surgery is required for patients whose origin of bleeding is identified and can only be treated with surgical intervention. (3)
- Other treatment methods Extracorporeal membrane oxygenation can be a lifesaving strategy in pa-

tients with severe lung injury and profound hypoxemia. (10)

5 | APPROACH TO NON-LIFE-THREATENING HEMOPTYSIS

5.1 | History & Physical Examination

The patient's history must include an assessment of the frequency, severity, and the quantity of the hemoptysis. Associated symptoms, comorbidities, and risk factors for lung cancer including smoking and exposure to asbestos should be explored. (2) Certain historical findings can help narrow down the differential diagnosis. (3, 4)

A review of medications with a focus on anticoagulants and family history of bleeding disorders can assess the possibility of coagulopathy. Cough can be associated with bronchiectasis, chronic obstructive pulmonary disease (COPD), foreign body aspiration, pneumonia, and tuberculosis (TB). (4) The presence of fever can suggest bronchitis, pneumonia, lung abscess, neoplasm, pulmonary embolism (PE), and TB. (4) Sputum production is found in patients presenting with bronchiectasis, COPD, pneumonia, and TB. (4) History of smoking can be suggestive of bronchitis, COPD, and neoplasm. (4)

Immunosuppressed patients are at increased risk of lung abscess, pneumonia, and TB. (4) Recent diagnostic manipulation in the airways or foreign body aspiration could be a source of injury and subsequent infection (1). If the patient has been recently immobilised, PE should be considered. (3, 4)

The physical examination consists of evaluating the degree of respiratory distress (presence of tachypnea, cyanosis, use of accessory muscles of respiration) and the hemodynamic stability of the patient. We can also look for cues of pulmonary disease, cardiac disease, and other systemic diseases. (2) Clubbing of the digits is found in patients with lung cancer. Asymmetric peripheral edema can indicate the presence of deep vein thrombosis.

5.2 | Imaging

5.2.1 CXR is suggested as a first-line investigation for all patients with hemoptysis. (5) It is quick, readily available, and cheap. It determines the site of bleeding in 45-65% of the cases and is the cause in 25-35% of the cases. (1)

For patients with normal CXR presenting with minimal hemoptysis, a likely infectious or a benign cause, and no risk factors for lung malignancy, further evaluation can be deferred. (2) Patients with a suspected viral infection are observed and patients with a suspected bacterial infection are treated with antibiotics. (2) In case of recurrence or persistence of the hemoptysis, further investigation with CT or bronchoscopy is needed.

For patients with normal CXR presenting with active hemoptysis, without a clear or benign cause, a CT scan with contrast is warranted. If a clear diagnosis is not established, flexible bronchoscopy can be considered. (2)

For patients with normal CXR presenting with recurrent hemoptysis, a CT scan is recommended. (2) The most common causes for recurrent hemoptysis in patients with a normal CXR are bronchiectasis, carcinoid tumors, catamenial hemoptysis, and pulmonary arteriovenous malformation. (2) Pulmonary malignancies can be found in 10% of patients with risk factors for lung cancer who present with a normal CXR. (1)

- **5.2.2** CT scan with contrast is recommended for investigation of the origin and the etiology of hemoptysis. (10) Analysis of thin sections is necessary to adequately evaluate for bronchiectasis. (1) CT can help guide an embolization procedure to treat the hemoptysis. (1) PE is a rare cause of hemoptysis and when suspected should be evaluated with CT pulmonary angiography. (2)
- 5.2.3 Flexible bronchoscopy can be performed at the bedside and can be useful in securing the patient's airway if necessary. (1, 10) It also allows for endo-bronchial treatment procedures and obtaining pathologic or cytologic specimens. (2)

- 5.3.1 Hemoglobin and hematocrit can assist in assessing the chronicity and/or severity of the blood loss. Again, note that the main danger of acute hemoptysis is asphyxiation rather than blood loss. (2)
- **5.3.2** White blood cell count and differential can indicate the presence of an infection. (2)
- **5.3.3** Urinalysis and renal function tests are useful in screening for pulmonary renal syndromes including anti-glomerular basement membrane disease and granulomatosis with polyangiitis. (2)
- **5.3.4** Liver function tests and a coagulation profile are helpful in evaluating thrombocytopenia and other bleeding disorders. (2)
- **5.3.5** Sputum culture including mycobacterial culture can be ordered, when infectious etiology is suspected. (2) If TB is suspected, acid-fast bacillus smear should be done 3 times, as well as PCR test when available.
- 5.3.6 Serologic testing such as antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), anti-glomerular basement membrane (anti-GBM) antibodies, and antiphospholipid (APS) antibodies can be useful when autoimmune diseases are suspected, including systemic lupus erythematosus, granulomatosis with polyangiitis, anti-glomerular basement membrane disease and antiphospholipid antibody syndrome. (2)

5.4 | Management of Non-Life-Threatening Hemoptysis

The management of non-LTH consists of treating the underlying etiology. For instance, patients with infiltrate seen on CXR and signs and symptoms suggestive of pneumonia should be treated with antibiotics. (4) If viral etiology is suspected, the patient's condition should be observed. In the case of PE, the patient should be treated with anticoagulation. (12) Patients with COPD or bronchiectasis can be referred to respiratory medicine where they can be further assessed and treated. Importantly, non-LTH does not equate to non-

life-threatening pathology. While certain pathologies may not present as imminent hemorrhage or asphyxiation, they may evolve into life-threatening pathologies (i.e. tracheoinnominate fistula).

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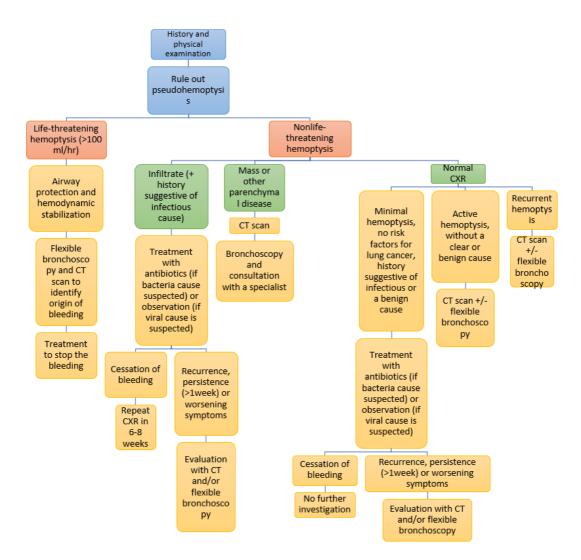
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FLOWCHART 1 Approach to hemoptysis